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BAU 1643  
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Jina C.  
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Dkt. 30634-B/JPW/JML/YL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Eric Rose, et al.

Serial No. : 09/053,872

Filed : April 1, 1998 Art Unit: 1643

For : METHODS FOR INHIBITING THROMBOSIS IN A  
PATIENT WHOSE BLOOD IS SUBJECTED TO  
EXTRACORPOREAL CIRCULATION

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1185 Ave. of the Americas  
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Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents, which are listed on Form PTO-1449 and are also listed below. Copies of the documents were previously submitted in connection with copending, coassigned, U.S. Serial No. 08/648,561, filed May 16, 1996, of which the above identified patent application is a continuation-in-part. The documents listed herebelow as items 1-14 are again listed on Form PTO-1449 which is attached hereto as Exhibit 1.

1. Bazan, J. F., Big rigs in blood coagulation, Nature 380:21-23, 03/1996;
2. Benedict, C.R. et al., Active site-blocked factor IXa prevents intravascular thrombus formation in the coronary vasculature without inhibiting extravascular coagulation in a canine thrombosis model, J. Clin. Invest., 88:1760-1765, 1991;

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Page 2

3. Benedict, C. R., et al., Endothelial-Dependent Procoagulant and Anticoagulant Mechanisms, Texas Heart Institute Journal, 21: 86-90, 1994;
4. Berntorp, E., Biochemical and in vivo properties of high purity factor IX concentrates, Thrombosis and Haemostasis 70(5):768-773, 11/1993;
5. Freedman, S.J. et al., Structure of the metal-free  $\gamma$ -carboxyglutamic acid-rich membrane binding region of factor IX by two-dimensional NMR spectroscopy, J. Biol. Chem., 270(14):7980-7987, 04/1995;
6. Furie, B.C. and Furie, B. (1995) Biosynthesis of factor IX: implications for gene therapy, Thrombosis and Haemostasis, 74(1):274-277;
7. Iberti, T.J. et al., Abnormal coagulation profile in brain tumor patients during surgery, Neurosurgery, 34(3):389-395, 03/1994;
8. Kirchhofer, et al. (1995) Active site-blocked factors VIIa and IXa differentially inhibit fibrin formation in a human ex vivo thrombosis model, Arterioscler. Thromb. Vasc. Biol., 15:1098-1106;
9. Kuwabara, K. et al., Calreticulin, an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries, J. Biol. Chem., 270(14):8179-8187, 04/1995;

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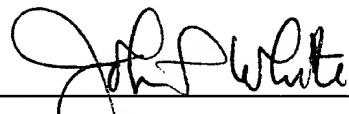
10. Miyata, T. et al., Factor IX Bm Kiryu: a Val-313-to-Asp substitution in the catalytic domain results in loss of function due to a conformational change of the surface loop: evidence obtained by chimeric modeling, Brit. J. Of Haematol., 88(1):156-165, 09/1994;
11. Santagostino, E. et al., Markers of hypercoagulability in patients with hemophilia B given repeated, large doses of factor IX concentrates during and after surgery, Thrombosis and Haemostasis, 71(6):737-40, 06/1994;
12. Wacey, A.I. et al., Determinants of the factor IX mutational spectrum in hemophilia B: an analysis of missense mutations using a multi-domain molecular model of the activated protein, Hum. Genet., 94(6):594-608, 12/1994;
13. Warrier, I. et al., Safety of high doses of a monoclonal antibody-purified factor IX concentrate, Am. J. Of Hematol., 49(1):92-94, 05/1995;
14. Wong, A. G. et al., Relative efficacy of active site-blocked factors IXa Xa in a model of venous thrombosis, Supplement I Circulation, Abstract # 3293 p. I-686, Vol. 92 No. 8, 10/1995;

Applicants request that the Examiner review the references and make them of record in the subject application.

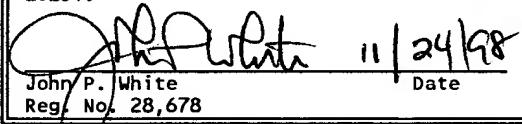
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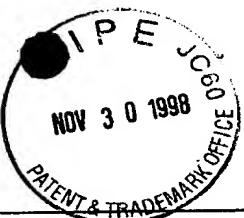
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any such fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231.	
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\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Exhibit 1



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Form PTO-1449 (Substituted)  
(Rev. 8-83)

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INFORMATION DISCLOSURE CITATION

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APPLICANTS  
Eric Rose, et al.

FILING DATE  
April 1, 1998

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1643 1653

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

JML	Benedict, C. R., et al., Endothelial-Dependent Procoagulant and Anticoagulant Mechanisms, <u>Texas Heart Institute Journal</u> , 21: 86-90, 1994;
	Berntorp, E., Biochemical and in vivo properties of high purity factor IX concentrates, <u>Thrombosis and Haemostasis</u> , 70(5):768-773, 11/1993;
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	Kirchhofer, et al. (1995) Active site-blocked factors VIIa and IXa differentially inhibit fibrin formation in a human <i>ex vivo</i> thrombosis model, <u>Arterioscler. Thromb. Vasc. Biol.</u> , 15:1098-1106;
JML	Kuwabara, K. et al., Calreticulin, an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries, <u>J. Biol. Chem.</u> , 270(14):8179-8187, 04/1995;
	Miyata, T. et al., Factor IX Bm Kiryu: a Val-313-to-Asp substitution in the catalytic domain results in loss of function due to a conformational change of the surface loop: evidence obtained by chimeric modeling, <u>Brit. J. Of Haematol.</u> , 88(1):156-165, 09/1994;

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JL	Santagostino, E. et al., Markers of hypercoagulability in patients with hemophilia B given repeated, large doses of factor IX concentrates during and after surgery, <u>Thrombosis and Haemostasis</u> , 71(6):737-40, 06/1994;
	Wacey, A.I. et al., Determinants of the factor IX mutational spectrum in hemophilia B: an analysis of missense mutations using a multi-domain molecular model of the activated protein, <u>Hum. Genet.</u> , 94(6):594-608, 12/1994;
JL	Warrier, I. et al., Safety of high doses of a monoclonal antibody-purified factor IX concentrate, <u>Am. J. Of Hematol.</u> , 49(1):92-94, 05/1995;
	Wong, A. G. et al., Relative efficacy of active site-blocked factors IXa Xa in a model of venous thrombosis, <u>Supplement I Circulation</u> , Abstract # 3293 p. I-686, Vol. 92 No. 8, 10/1995;

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